

REMARKS

Entry of the foregoing amendment and favorable consideration of the subject application is respectfully requested in view of the following comments.

Claims 1 and 4-9 are currently pending in the subject application. By the foregoing amendment, claim 1 has been amended to recite the specific structure of the anion-exchange and cation-exchange membranes and claim 6 has been amended to recite the structure of the medical instrument specifying the arrangement of the membranes with respect to a surface of a living body and the working electrode. Claim 8 has been cancelled.

Specifically, claim 1 has been amended to more positively recite a medical instrument for transdermally administering a medicine comprising a bag and an ionic medicine or an ionic medicine-containing substance sealed in the bag, wherein the bag comprises an anion exchange membrane and a cation exchange membrane which are melt-adhered to each other along the peripheral edges thereof wherein the anion and cation-exchange membranes comprise a sheet or film of a porous thermoplastic resin with at least part of the pores or voids being filled with an ion exchange resin. This is the preferred form of the membrane as disclosed in the specification at page 10, line 5 to page 13, line 1. The inclusion of the ion exchange resin in the pores of the membrane makes possible the maintenance of close

contact with the skin of a user and enhances the administration of medicine through the membrane.

Claim 6 has been amended to recite the structure of the medical device of claim 1 wherein the arrangement is such that the anion or cation-exchange membrane which permeates ions of the same polarity as the pharamacologically effective ions of the medicine is capable of coming in contact with the skin, while the anion or cation-exchange membrane which permeates ions of opposite polarity is connected to the working layer of the device through an electrolyte layer. The latter feature was previously recited in claim 8 which is cancelled herein.

Applicants respectfully submit that no new matter has been entered in this amendment and that the subject application is in condition for allowance.

Rejection of Claims 1 & 4-6 under 35 U.S.C. § 103(a)

The Office Action rejects claims 1 and 4-6 under 35 U.S.C. § 103(a) as being unpatentable over Matsumura et al (US Pub. No. 2005/0070840A1) in view of Sibalís US Patent No. 4713050). The Office Action states:

The Matsumura et al reference discloses an iontophoresis device that has an working electrode 11 connected to a medical instrument (13, 14, 15), consisting of a anion-exchange membrane & a cation-exchange membrane connected to a ionic medicine, and a counter electrode 21 connected to the working electrode 11 through a cell 3 and utilizes a electrolyte layer 12 to connect the working electrode 11 to a medical

instrument (13,14,15). The Matsumura reference clearly shows the anion membrane and the cation membrane surrounding the ionic medicine. Now even though Matsumura does not explicitly disclose the medicine sealed in a bag attention is directed to Sibalis. The Sibalis reference teaches a device that utilizes medicine, which can be sealed in a bag, see col. 3, lines 22-41. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura et al with the device of Sibalis in order to create a bag for the medication that is to be delivered that prevents leakage of the drug and to help contain the drug. Also wherein the "... by melt adhering ..." is deemed to be written in product by process language and since the bag is sealed it would inherently be able to have been sealed by that process, also it would be obvious for one of ordinary skill in the art to utilize melt-adhering to seal and form the bag since it is well known to do so not just in the medical art but also generally in sealing bags.

With respect to claim 4, wherein the ionic-medicine substance is a sheet impregnated with a solution of an ionic medicine, see para [0121] Matsumura.

Applicants respectfully traverse the rejection because the *prima facie* case of obviousness has not been established with respect to the presently pending claims 1 and 4-6.

The Federal Circuit has ruled that a *prima facie* case of obviousness must establish: (1) some suggestion or motivation to modify the references; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all claim limitations. Amgen, Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Feb. Cir. 1991); In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established as there is no convincing line of reasoning which would lead one of ordinary skill in the art to apply the teachings of Sibalis to modify the device of Matsumura, et al., to obtain the medical instrument as now recited in the claims amended herein.

Although disclosing a basic structure of an iontophoresis device, Matsumura does not describe or suggest sealing an ionic medicine in a bag comprising an anion exchange membrane and a cation exchange membrane sealed as recited in the present claims.

In the present invention, an ionic medicine is sealed in a bag which comprises an anion exchange membrane and a cation membrane wherein the membranes are sealed to each other along their peripheral edges by melt adhering. In this manner, the medicine necessary for iontophoresis and the ion exchange membrane are provided as a single, compact structure which is

portable and easily handled. Furthermore, since the bag containing the medicine is formed from the ion exchange membrane, a separate ion exchange structure between the bag and the patient's skin is not necessary thereby permitting the transdermal instrument to more favorably conform to the patient's skin for effective administration of the medicine.

Matsumura merely discloses stacked layers of membrane bodies and fails to disclose or suggest the structure of the present claims comprising a sealed bag containing an ionic medicine for transdermal administration.

Furthermore, Matsumura fails to disclose or suggest anion-exchange or cation-exchange membranes having the structure recited in claim 1 as now amended. Specifically, Matsumura fails to disclose such membranes comprising porous thermoplastic resins having a porosity of from 20% to 95% with the pores being filled by an ion-exchange resin in a filling ratio of from 5% to 95% by weight.

As for Sibalis, Applicants respectfully point out that this reference fails to cure the above noted defect in the teaching of Matsumura. Although Sibalis discloses an iontophoresis device provided with a reservoir 24, the walls of which are sufficiently dense to prevent leakage of the drug contained therein but sufficiently porous to permit migration of charged particles or ions under the influence of an electric field, there is no

disclosure in Sibalis which either teaches or suggests that those walls comprise a porous thermoplastic resin having a porosity of 20% to 95% and a cross-linked ion-exchange resin filling said pores in a filling ratio of from 5% to 95% by weight.

At best, Sibalis teaches the inclusion of a separate and distinct element, i.e., microporous or semi-permeable membrane 22, which is disposed between the reservoir and the skin. Applicants respectfully submit that modification of Matsumura according to the teaching of Sibalis as suggested by the examiner not only would not result in the structure of the anion-exchange and cation-exchange membrane of the present invention, but would also prevent direct contact between the membranes of the present invention and the skin of a patient, as recited in claim 6, by the imposition of the membrane 22 of Sibalis between the anion-exchange or cation-exchange membranes and the skin.

In view of the foregoing, Applicants respectfully submit that the examiner's rejection of claims 1 and 4-6 as obvious over Matsumura in view of Sibalis has been overcome and that a *prima facie* case of obviousness has not been established. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejection of Claims 7-9 under 35 U.S.C. § 103(a)

Claims 7-9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumura et al (US Pub No.

2005/0070840A1) in view of Sibalis (US Patent No. 4713050) as applied to claim 6 and further in view of Theeuwes et al (U.S. Patent No. 5169382). The Office Action states:

Now even though the device of Matsumura in view of Sibalis does not explicitly disclose the use of a flexible armoring member for the electrodes attention is directed to Theeuwes. The Theeuwes reference teaches a flexible armoring member 22 in figure 1 on the device. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura with the device of Theeuwes in order to provide a flexible protecting member for protecting the components of the device from damage.

With respect to claims 8-9, wherein the electrolyte layer connects the working electrode to the medical instrument, see figures 3 & 4 of Matsumura, and wherein the layer is in the form of a paste or a gel, see para [0122] Matsumura.

Applicants respectfully traverse the rejection because the *prima facie* case of obviousness has not been established with respect to the presently pending claims 7 and 9. Cancellation of claim 8 renders this rejection as to that claim moot.

As previously pointed out, the Federal Circuit has ruled that a *prima facie* case of obviousness must establish: (1) some suggestion or motivation to modify the references; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all claim limitations. Amgen, Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Feb. Cir. 1991); In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165

USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

For the reasons given above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established as there is no convincing line of reasoning which would lead one of ordinary skill in the art to apply the teachings of Sibalis to modify the device of Matsumura, et al., to obtain the medical instrument as now recited in the claims amended herein.

As to the application of Theeuwes for the teaching of a flexible armoring member, Applicants respectfully submit that since claims 7 and 9 are ultimately dependent from claim 1 as requiring the device recited therein, the examiner's rejection is further traversed because Theeuwes fails to disclose or suggest a membrane structure for the

anion-exchange and cation-exchange membranes which make up the bag of the present invention.

Furthermore, claims 7 and 9 depend from claim 6 which recites the anion-exchange membrane or the cationic-exchange membrane which permeates ions of the same polarity as pharmacologically effective ions of the membrane as capable of coming in contact with a surface of a living body.

Theeuwes, on the other hand, is directed to a membrane capable of inhibiting agent release from a delivery system and specifically discloses that this membrane is positioned between a drug reservoir and the body surface and, as such, it is not possible for the membranes which comprise the reservoir of Theeuwes to come in contact with the body surface. Accordingly, the modification of Matsumura as suggested by the examiner is not only not obvious, but the secondary reference to Theeuwes teaches against such modification since the invention as recited in claims 7 and 9 of the present application would require elimination of the specific object of the Theeuwes reference in order to comply with the recitation of claim 6 from which they depend.

Because of the inclusion of the limitations of claims 1 and 6 into claims 7 and 9, and the failure of the cited

references to disclose or suggest all of those limitations, Applicants respectfully submit that the examiner's present ground for rejection as based on the teaching in Theeuwes of a flexible armoring member 22 in figure 1 is moot. As pointed out above, the secondary reference fails to disclose or suggest the structure of the anion-exchange or cation-exchange membranes of the present invention as recited in claim 1 herein nor the arrangement as recited in claim 6. Thus, the secondary reference fails to cure the deficiencies of Matsumura and Sibalis.

In view of the foregoing, Applicants respectfully submit that the examiner's rejection of claims 7 and 9 as obvious over Matsumura in view of Sibalis as applied to claim 6 and further in view of Theeuwes, has been overcome and that a *prima facie* case of obviousness has not been established. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejection of Claims 1, 4-6 under 35 U.S.C. § 103(a)

Claims 1, 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumura et al (US Pub. No. 2005/0070840A1) in view of Kedem et al (US Patent No. 4217200). The Office Action States:

Matsumura et al. reference discloses an iontophoresis device that has an working electrode 11

connected to a medical instrument (13, 14, 15), consisting of a anion-exchange membrane & a cation-exchange membrane connected to a ionic medicine, and a counter electrode 21 connected to the working electrode 11 through a cell 3 and utilizes a electrolyte layer 12 to connect the working electrode 11 to a medical instrument (13, 14, 15). Now even though Matsumura does not explicitly disclose the use of utilizing an ion-exchange membrane bag attention is directed to Kedem. The Kedem reference teaches the use of heat-sealed anion-exchange membrane & cation-exchange membrane bags see col. 1 line 35 - col. 2 line 26. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura with the device of Kedem in order to provide a convenient disposable and/or interchangeable medical instrument and for providing a dual sided ion exchange membrane.

Applicants respectfully traverse the rejection because the *prima facie* case of obviousness has not been established with respect to the presently pending claims 1 and 4-6.

For the reasons given above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established as there is no convincing line of reasoning which would lead one of ordinary skill in the art to apply the teachings of Kedem to modify the device of Matsumura, et al., to obtain the medical instrument as now recited in the claims amended herein.

Although disclosing a basic structure of an iontophoresis device, Matsumura does not describe or suggest sealing an ionic medicine in a bag which comprises an anion exchange membrane and a cation exchange membrane having the structure recited in the present claims.

In the present invention, an ionic medicine is sealed in a

bag which comprises an anion exchange membrane and a cation membrane wherein the membranes are sealed to each other along their peripheral edges by melt adhering. In this manner, the medicine necessary for iontophoresis and the ion exchange membrane are provided as a single, compact structure which is portable and easily handled. Furthermore, since the bag containing the medicine is formed from the ion exchange membrane, a separate ion exchange structure between the bag and the patient's skin is not necessary thereby permitting the transdermal instrument to more favorably conform to the patient's skin for effective administration of the medicine.

Matsumura merely discloses stacked layers of membrane bodies and fails to disclose or suggest the structure of the present claims comprising a sealed bag containing an ionic medicine for transdermal administration.

Furthermore, Matsumura fails to disclose or suggest anion-exchange or cation-exchange membranes having the structure recited in claim 1 as now amended. Specifically, Matsumura fails to disclose such membranes comprising porous thermoplastic resins having a porosity of from 20% to 95% with the pores being filled by an ion-exchange resin in a filling ratio of from 5% to 95% by weight. Thus, Matsumura fails to disclose or suggest the present invention.

With regard to Kedem, et al., the examiner contends that

this reference teaches the use of anion exchange membrane and cation exchange membrane bags, citing col. 1, line 35-col. 2, line 26, and that it would be obvious to one of ordinary skill in the art to modify the device of Matsumura, et al., with the device of Kadem in order to provide a convenient disposable and/or interchangeable medical instrument.

Applicants respectfully point out that the device of Kadem, et al., consists of a type of membrane unit for use in electrodialysis and desalination devices. As such, they essentially constitute filtration units and require an entrance and an exit as is clearly noted in the Summary of the Invention referred to by the examiner. Indeed, Kadem further discloses that the membranes form "... an integral unit with a frame, which frame is characterized in that it can be attached by heat-sealing to similar frames of other membranes ..." (Col. 1, lines 37-40). Thus, Kadem requires structure that is inconsistent with an iontophoresis device, i.e., a frame about the peripheral edges between the membranes and inlet and outlet structures to permit the flow of dialysate through the cells formed from the framed membrane structures. Accordingly the structure and purpose of Kadem, et al. is different from the device as recited in the present claims and Applicants respectfully submit that it would not be obvious to apply the teachings of Kadem, et al., as employed in a device relying on a counter-current flow of

dialysate and electrolyte through a filtration unit to an iontophoretic device for direct transdermal administration of medicine to a patient.

Furthermore, Kedem fails to disclose or suggest the structure of the anion-exchange and cation-exchange membranes as recited in the claims amended herein. Specifically, there is no suggestion that such membranes comprise "a film or sheet of a porous thermoplastic resin having a porosity of from 20% to 95%, and a cross-linked ion-exchange resin in the pores of said thermoplastic resin in a filling ratio of from 5% to 95% by weight, wherein said cross-linked ion-exchange resin is a cation-exchange resin or an anion-exchange resin as determined by the ionic medicine to be administered".

Accordingly, Applicants respectfully submit that the rejection of claims 1, 4-6 as unpatentable over Matsumura, et al., in view of Kadem, et al., is not supported by the references and should be withdrawn.

In light of the foregoing, Applicants submit that a prima facie case of obviousness has not been sufficiently established in the present application and that the application is now in condition for allowance. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of the pending claims and allow the pending claims. Favorable action with an

early allowance of the claims pending is earnestly solicited.

Respectfully submitted,

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